Study of serum vitamin B12 levels in pregnant mothers and their newborns and its relation to growth of the infants

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ABSTRACT

Introduction: The effect of vitamin B12 deficiency in pregnancy on the growth of infants has not been properly studied. **Objectives:** To study the correlation of vitamin B12 levels in pregnant mothers with vitamin B12 levels in their newborn infants and to know it's relation to the growth of infants. **Materials and Methods:** Hundred full-term pregnant women and their newborns were enrolled from January 2011 to January 2012. Vitamin B12 levels were assessed and the growth of infants monitored till 6 months of age. **Results:** A total of 60 pregnant women (60%) had vitamin B12 deficiency while 29 newborns (29%) had low vitamin B12 levels. Vitamin B12 levels in the newborns had a strong positive correlation with mothers' vitamin B12 levels ($r=0.56$; $p<0.05$). Babies born to vitamin B12 deficient mothers were shorter, and their mean weight at 6-month of age was significantly less. **Conclusion:** Vitamin B12 deficiency is very common in Indian pregnant mothers; it leads to vitamin B12 deficiency and growth retardation in their babies.

Keywords: *Growth retardation, Newborns, Pregnant women, Vitamin B12*

Vitamin B12 is a water-soluble vitamin and can be stored in the liver. Vitamin B12 is very essential for hematopoiesis and neurological function. Vitamin B12 is naturally found in animal products such as meat, dairy products, and eggs. People on strict vegetarian or vegan diets may become deficient in vitamin B12 if adequate fortified foods or supplements are not consumed [1]. The quality of diets in low-income populations in developing countries is compromised by limited access to high-cost, nutrient-rich foods, and especially animal source foods which are a rich source of vitamin B12 [1-3].

The prevalence of vitamin B12 deficiency in Indian women is around 47-50%. The most frequent cause of vitamin B12 deficiency is inadequate intake, unlike developed countries. The most important cause of vitamin B12 deficiency in infants is a maternal dietary deficiency. It is generally observed in an infant who's mothers are deficient in vitamin B12 store [4,5]. When the vitamin B12 status of women is poor during pregnancy and lactation, their infants may have smaller stores of the vitamin B12 at birth [6], and the concentration of the vitamin B12 in breast milk is likely to be low [7].

In India, the dietary intake of animal protein food in the majority of the population is very low, either because of religious conviction or because of its high cost leading to the lesser intake of meat or milk products [8]. Hence, probably the burden of vitamin B12 deficiency is very high in India, and this could be contributing to large incidence of growth retardation in children. To study this aspect in detail, we planned this prospective study.

MATERIALS AND METHODS

This longitudinal study was conducted over a period of 1 year from January 2011 to January 2012 after obtaining ethical clearance. Hundred mothers with their newborn were enrolled in the study after admission in tertiary care hospital in Southern India. After taking written informed consent, mothers and their newborns who fulfilled the inclusion criteria were included in the study. Healthy term gestation mothers who delivered normally, a healthy newborn that was exclusively breastfed was included in the study. A complete history taking, physical examination, and relevant laboratory evaluation were done. Blood for the serum vitamin B12 was drawn just before the delivery in mothers and on the 2nd day of life in their newborns.

A serum separator tube was used, and 3 ml blood samples were allowed to clot for 2 h at room temperature or overnight before centrifugation for 20 min. Vitamin B12 estimation was done by the competitive inhibition enzyme immunoassay technique [9]. Anemia in mother was defined according to WHO classification [10]. Socioeconomic status was classified using the modified BG Prasad classification.

The comparison of categorical data was done using Chi-square test and Fisher exact test while the continuous data were analyzed

using student t-test and ANOVA. The Pearson's correlation coefficient was used to establish the correlation of between two variables. p≤0.05 was considered as statistically significant. SPSS version 19.0 software was used for the statistical analysis.

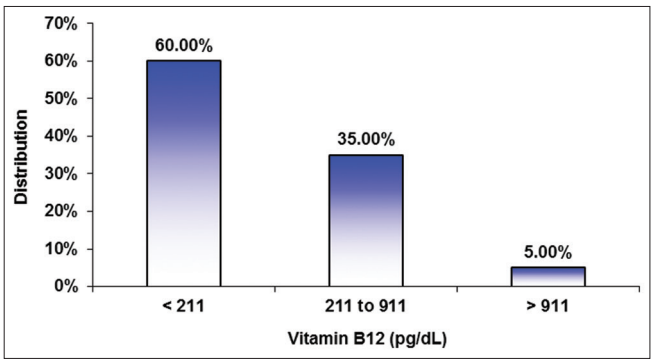
RESULTS

A total of 60 (60%) mothers had vitamin B12 deficiency (<211 pg/dl) (Graph 1) and among the newborns, 29 (29%) babies had low vitamin B12 level (<211 pg/dl) (Graph 2). 72 (72%) mothers belonged to 20-25 year age group, and 81 (81%) mothers weighed between 50 and 70 kg. All the mothers were equally distributed among the various socioeconomic classes from I to IV (30% in Class I, 22% in Class II, and 24% each in Class III and IV). 82 (82%) mothers used to take non-vegetarian occasionally while the remaining 18% were strictly vegetarian. 48 (48%) of women were primiparous. Anemia (Hb <11 mg/dl) was present in 53% of mothers, and only 6% of mother's peripheral smear showed dimorphic anemia.

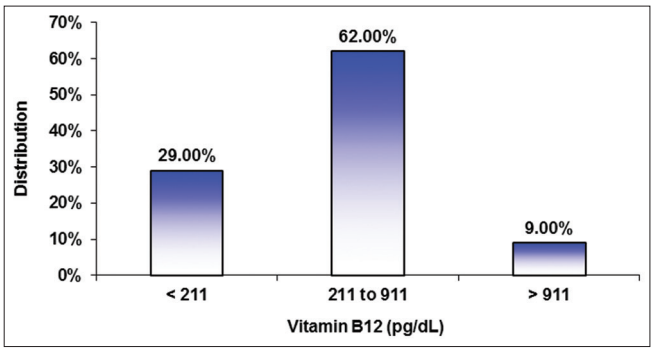
Of the 100 newborns, 57% were boys, and 43% were girls. Mean head circumference (HC) of babies at birth was 33.64±1.16 cm, at 3rd month was 39.38±1.50 cm, and at the 6th month was 42.55±2.44 cm. The mean length of babies at birth was 48.60±2.50 cm, at 3rd month was 57.62±2.95 cm, and at the 6th month was 63.51±3.81 cm. The mean weight of babies at birth was 2898±540.12 g, at 3rd month was 5436.40±656.49 g, and at the 6th month was 6820.50±734.16 g as shown in Table 1. Linear scattered correlation graph showed a strong positive correlation between vitamin B12 levels in mother and their babies (r=0.56) (Graph 3).

At birth, all the babies born to normal vitamin B12 levels mothers (X) had higher mean HC (33.87±1.21 vs. 33.5±1.15 cm), mean length (49.94±3.24 vs. 48.19±2.40 cm), and mean weight (3080.00±356.37 vs. 2841.67±603.83 g) than those born to lower vitamin B12 level mothers (X1) but statistically significant difference was found only in case of mean length (p=0.02). At 3 months, babies born to normal Vitamin B12 mothers had higher mean HC (39.70±1.20 vs. 39.18±1.68 cm), mean length (58.67±3.46 vs. 56.99±2.48 cm), and mean weight (5760.00±589.92 vs. 5244.00± 709.96 g) than those born to lower vitamin B12 level mothers but statistically significant difference was found in case of mean length (p=0.001) and mean weight (p=0.02).

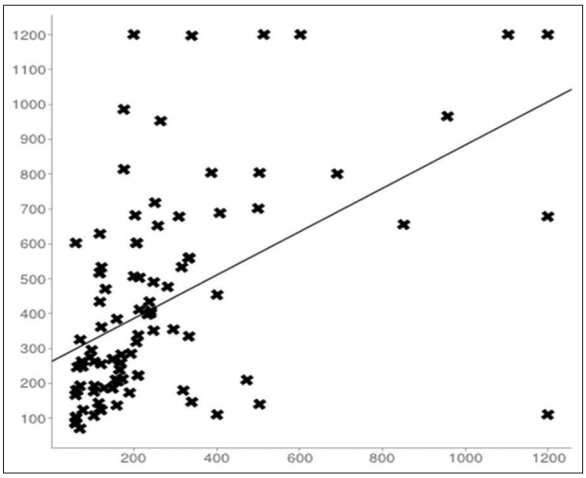
At 6 months, babies born to normal vitamin B12 mothers had higher mean length (64.20±2.17 vs. 63.1±4.30 cm), mean weight (7320.00±554.08 vs. 6679.17±712.79 g) than those born to lower vitamin B12 level mothers. The mean HC was almost similar in both groups. The statistical significant difference was seen in case of mean weight (p=0.03).



Graph 1: Vitamin B12 levels in pregnant mothers. Two-thirds of otherwise healthy pregnant mothers had low vitamin B12 levels



Graph 2: Bar diagram showing vitamin B12 levels in newborn babies. One-third babies had low vitamin B12 levels at birth



Graph 3: Correlation of vitamin B12 levels in mother and child. X axis: Mother's vitamin B12 level. Y axis: Baby's vitamin B12 level. Correlation coefficient (r): 0.52. There is a positive correlation between the vitamin B12 levels in mother and their babies

DISCUSSION

Vitamin B12 is a water-soluble vitamin and is necessary for the production of tetrahydrofolate, which is essential for DNA synthesis. Vitamin B12 deficiency often presents with nonspecific manifestations, such as developmental delay, irritability, weakness, and failure to thrive and is difficult to diagnose by pediatricians [11]. It also presents as megaloblastic anemia and hyperpigmentation of skin with sparse lusterless hair.

The most common cause of vitamin B12 deficiency in infants is a dietary deficiency in the mothers [11]. Strict vegetarians and even omnivores, who consume low amounts of animal products, are more likely to become vitamin B12 deficient during pregnancy, lactation and give birth to infants with diminished vitamin B12 stores. Exclusive breastfeeding of these infants

Table 1: Anthropometric parameters with age in babies born to mothers with vitamin B12 deficiency and normal vitamin B12 levels

Age	Anthropometric parameter	Normal vitamin B12 levels	Low vitamin B12 levels	p value
At birth	Mean weight (g)	3050.00±356.37	2841.67±603.83	>0.05
	Mean length (cm)	49.94±3.24	48.19±2.40	0.02
	Mean HC (cm)	33.87±1.21	33.50±1.15	>0.05
3 months	Mean weight (g)	5760.00±589.92	5244.00±709.96	0.02
	Mean length (cm)	58.67±3.46	56.99±2.48	0.001
	Mean HC (cm)	39.70±1.20	39.18±1.68	>0.05
6 months	Mean weight (g)	7320.00±554.08	6679.17±712.79	0.03
	Mean length (cm)	64.20±2.17	63.10±4.30	>0.05
	Mean HC (cm)	41.5±1.01	41.0±1.05	>0.05

Student t-test was used and p<0.05 is taken as statistically significant. HC: Head circumference

further contributes to the deficiency. One of the important reasons for maternal vitamin B12 deficiency in some developing countries is poor socioeconomic status [12]. Vitamin B12 deficiency in mothers can lead to babies who are intrauterine growth retarded (IUGR), but there is limited data on vitamin B12 levels in mother and the effect of the same on the neonate mainly in the form of few small studies and case reports.

This study was a prospective study of 100 mothers and their newborns to know the relation between vitamin B12 levels and growth of infants. Vitamin B12 deficiency was found in 60% of the mothers but only 19% of them showed a peripheral smear of megaloblastic anemia. Hence, a peripheral smear which is routinely done in pregnant mothers is not a sensitive method for picking up vitamin B12 deficiency in mothers [13]. Among the newborns, 29% were deficient in vitamin B12. Katre et al. study has also shown that 80% of rural and 65% of urban women had low vitamin B12 levels [14]. Koc et al. has shown 41% of newborns were deficient in vitamin B12 [15]. Baker et al. has shown that vitamin B12 levels in babies will be 1 to 2.3 times higher than mother's level, our study also has shown similar result [16]. There has been no study regarding the normal level of vitamin B12 in newborn. According to Baker et al. the levels in newborn are higher than in their mothers. If we take vitamin B12 cutoff range of 485 pg/ml (2.3 times higher than mother's cutoff 211 pg/dl) for newborns then 56% of newborns would have been deficient in vitamin B12 at birth, and 60% of mother were deficient in vitamin B12.

There was a strong positive correlation (r=0.56) between vitamin B12 levels in mothers and their babies. Koc et al. study have shown a statistically significant correlation between maternal and cord blood vitamin B12 levels (r=0.395). Our study reveals a strong positive correlation compared to Koc et al. [15]. In this study, demographic characteristics such as weight and socioeconomic status showed a positive association with vitamin B12 levels among mothers and their babies (p<0.050), Halicioglu et al. also showed that SE status has a positive correlation with vitamin B12 level [17]. Mother's age had an inverse association with vitamin B12 level of babies (p<0.001). Furthermore, the diet of mothers did not influence the vitamin B12 levels among mothers or babies (p>0.050).

Vitamin B12 levels of mothers and babies were significantly associated with anthropometry (p<0.05). Muthayya et al. have shown that low vitamin B12 levels in pregnant women can lead to IUGR babies which were correlating with our result [18]. He also showed that vitamin B12 levels in babies are significantly associated with low birth weight. Guez et al. reported a case of a child with microcephaly and developmental delay because of vitamin B12 deficiency [19]. Dagnelie et al. showed that low vitamin B12 can lead to stunting in children [20]. Halicioglu et al. showed that vitamin B12 deficiency in babies due to maternal deficiency might be a serious health problem in infants [21]. Therefore, screening and supplementation of pregnant and lactating women to prevent infantile vitamin B12 deficiency should be considered.

Small sample size and lack of treatment in those deficient in vitamin B12 were some of the limitations of this study. Recently, a study from Bengaluru, India, has demonstrated the effect of oral vitamin B12 in pregnant mothers in increasing the serum levels of vitamin B12 in mothers and their infants [22]. Even the weight of the babies of mothers who took supplemental vitamin B12 levels was more than those who did not receive vitamin B12. Thus, once we have data from a large number of centers from across the country, a Nationwide health policy of universal vitamin B12 supplementation in the lines of iron and folic acid supplementation can be made. For this similar studies like ours on a larger scale are needed from different centers.

CONCLUSION

The study results show that vitamin B12 deficiency is highly prevalent among pregnant women in this region and there is a strong positive correlation of vitamin B12 levels in mothers and their babies. Vitamin B12 deficiency in both mother and the baby is associated with lower length at birth and lower mean weight at 6 months of age. Routine screening and supplementation of a pregnant mother with vitamin B12 can be an important strategy to improve the growth of children in our country.

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